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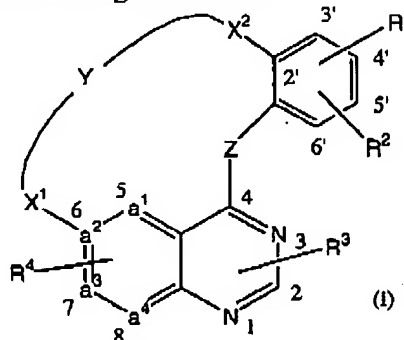
USSN 10/596,512  
Docket No. PRD2170USPCT

MAY 21 2008

**Listing of Claims:**

This listing of claims replaces all prior versions, and listings, of claims in the captioned application.

1. (Original) A compound having the formula



the *N*-oxide forms, the pharmaceutically acceptable addition salts and the stereochemically isomeric forms thereof, wherein

$a^1-a^2=a^3-a^4$  represents a divalent radical selected from  $N-CH=CH-CH$ ,  $N-CH=N-CH$  or  $CH-CH=N-CH$ ;

Z represents O, NH or S;

Y represents  $-C_{3-9}alkyl-$ ,  $-C_{3-9}alkenyl-$ ,  $-C_{1-5}alkyl-oxy-C_{1-5}alkyl-$ ,

$-C_{1-5}alkyl-NR^{13}-C_{1-5}alkyl-$ ,  $-C_{1-5}alkyl-NR^{14}-CO-C_{1-5}alkyl-$ ,

$-C_{1-5}alkyl-CO-NR^{15}-C_{1-5}alkyl-$ ,  $-C_{1-6}alkyl-CO-NH-$ ,

$-C_{1-6}alkyl-NH-CO-$ ,  $-CO-NH-C_{1-6}alkyl-$ ,  $-NH-CO-C_{1-6}alkyl-$ ,  $-CO-C_{1-7}alkyl-$ ,

$-C_{1-7}alkyl-CO-$ ,  $C_{1-6}alkyl-CO-C_{1-6}alkyl$ ;

$X^1$  represents a direct bond, O,  $-O-C_{1-2}alkyl-$ , CO,  $-CO-C_{1-2}alkyl-$ ,  $NR^{11}$ ,

$-NR^{11}-C_{1-2}alkyl-$ ,  $NR^{16}-CO-$ ,  $NR^{16}-CO-C_{1-2}alkyl-$ ,  $-O-N=CH-$  or  $C_{1-2}alkyl$ ;

$X^2$  represents a direct bond, O,  $-O-C_{1-2}alkyl-$ , CO,  $-CO-C_{1-2}alkyl-$ ,  $NR^{12}$ ,

$NR^{12}-C_{1-2}alkyl-$ ,  $NR^{17}-CO-$ ,  $NR^{17}-CO-C_{1-2}alkyl-$ ,  $Het^{20}-C_{1-2}alkyl-$ ,  $-O-N=CH-$  or

$C_{1-2}alkyl$ ;

$R^1$  represents hydrogen, cyano, halo, hydroxy, formyl,  $C_{1-6}alkoxy-$ ,  $C_{1-6}alkyl-$ ,

$C_{1-6}alkoxy-$  substituted with halo,

$C_{1-4}alkyl$  substituted with one or where possible two or more substituents selected from hydroxy or halo;

$R^2$  represents hydrogen, cyano, halo, hydroxy, hydroxycarbonyl-,  $Het^{16}$ -carbonyl-,

$C_{1-4}alkyloxycarbonyl-$ ,  $C_{1-4}alkylcarbonyl-$ , aminocarbonyl-, mono-or

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di(C<sub>1-4</sub>alkyl)aminocarbonyl-, Het<sup>1</sup>, formyl, C<sub>1-4</sub>alkyl-, C<sub>2-6</sub>alkynyl-, C<sub>3-6</sub>cycloalkyl-,

C<sub>3-6</sub>cycloalkyloxy-, C<sub>1-6</sub>alkoxy-, Ar<sup>5</sup>, Ar<sup>1</sup>-oxy-, dihydroxyborane,

C<sub>1-6</sub>alkoxy- substituted with halo,

C<sub>1-4</sub>alkyl substituted with one or where possible two or more substituents selected from halo, hydroxy or NR<sup>5</sup>R<sup>6</sup>,

C<sub>1-4</sub>alkylcarbonyl- wherein said C<sub>1-4</sub>alkyl is optionally substituted with one or where possible two or more substituents selected from hydroxy or C<sub>1-4</sub>alkyl-oxy-;

R<sup>3</sup> represents hydrogen, C<sub>1-4</sub>alkyl, cyano or C<sub>1-4</sub>alkyl substituted with one or more substituents selected from halo, C<sub>1-4</sub>alkyloxy-, amino-, mono- or di(C<sub>1-4</sub>alkyl)amino-, C<sub>1-4</sub>alkyl-sulfonyl- or phenyl;

R<sup>4</sup> represents hydrogen, hydroxy, Ar<sup>3</sup>-oxy, Ar<sup>4</sup>-C<sub>1-4</sub>alkyloxy-, C<sub>1-4</sub>alkyloxy-, C<sub>2-4</sub>alkenyloxy- optionally substituted with Het<sup>12</sup> or R<sup>4</sup> represents C<sub>1-4</sub>alkyloxy substituted with one or where possible two or more substituents selected from C<sub>1-4</sub>alkyloxy-, hydroxy, halo, Het<sup>2</sup>-, -NR<sup>7</sup>R<sup>8</sup>-, carbonyl- NR<sup>9</sup>R<sup>10</sup> or Het<sup>3</sup>-carbonyl-;

R<sup>5</sup> and R<sup>6</sup> are each independently selected from hydrogen or C<sub>1-4</sub>alkyl;

R<sup>7</sup> and R<sup>8</sup> are each independently selected from hydrogen, C<sub>1-4</sub>alkyl, Het<sup>8</sup>, aminosulfonyl-, mono- or di (C<sub>1-4</sub>alkyl)-aminosulfonyl, hydroxy-C<sub>1-4</sub>alkyl-, C<sub>1-4</sub>alkyl-oxy-C<sub>1-4</sub>alkyl-, hydroxycarbonyl-C<sub>1-4</sub>alkyl-, C<sub>3-6</sub>cycloalkyl, Het<sup>9</sup>-carbonyl-C<sub>1-4</sub>alkyl-, Het<sup>10</sup>-carbonyl-, polyhydroxy-C<sub>1-4</sub>alkyl-, Het<sup>11</sup>-C<sub>1-4</sub>alkyl- or Ar<sup>2</sup>-C<sub>1-4</sub>alkyl-;

R<sup>9</sup> and R<sup>10</sup> are each independently selected from hydrogen, C<sub>1-4</sub>alkyl, C<sub>3-6</sub>cycloalkyl, Het<sup>4</sup>, hydroxy-C<sub>1-4</sub>alkyl-, C<sub>1-4</sub>alkyloxyC<sub>1-4</sub>alkyl- or polyhydroxy-C<sub>1-4</sub>alkyl-;

R<sup>11</sup> represents hydrogen, C<sub>1-4</sub>alkyl, Het<sup>5</sup>, Het<sup>6</sup>-C<sub>1-4</sub>alkyl-, C<sub>2-4</sub>alkenylcarbonyl- optionally substituted with Het<sup>7</sup>-C<sub>1-4</sub>alkylaminocarbonyl-, C<sub>2-4</sub>alkenylsulfonyl-, C<sub>1-4</sub>alkyloxyC<sub>1-4</sub>alkyl- or phenyl optionally substituted with one or where possible two or more substituents selected from hydrogen, hydroxy, amino or C<sub>1-4</sub>alkyloxy-;

R<sup>12</sup> represents hydrogen, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkyl-oxy-carbonyl-, Het<sup>17</sup>, Het<sup>18</sup>-C<sub>1-4</sub>alkyl-, C<sub>2-4</sub>alkenylcarbonyl- optionally substituted with Het<sup>19</sup>-C<sub>1-4</sub>alkylaminocarbonyl-, C<sub>2-4</sub>alkenylsulfonyl-, C<sub>1-4</sub>alkyloxyC<sub>1-4</sub>alkyl- or phenyl optionally substituted with one or where possible two or more substituents selected from hydrogen, hydroxy, amino or C<sub>1-4</sub>alkyloxy-;

R<sup>13</sup> represents hydrogen, C<sub>1-4</sub>alkyl, Het<sup>13</sup>, Het<sup>14</sup>-C<sub>1-4</sub>alkyl- or phenyl optionally substituted with one or where possible two or more substituents selected from hydrogen, hydroxy, amino or C<sub>1-4</sub>alkyloxy-;

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R<sup>14</sup> and R<sup>15</sup> are each independently selected from hydrogen, C<sub>1-4</sub>alkyl, Het<sup>15</sup>-C<sub>1-4</sub>alkyl- or C<sub>1-4</sub>alkyloxyC<sub>1-4</sub>alkyl-;

R<sup>16</sup> and R<sup>17</sup> are each independently selected from hydrogen, C<sub>1-4</sub>alkyl, Het<sup>21</sup>-C<sub>1-4</sub>alkyl- or C<sub>1-4</sub>alkyloxyC<sub>1-4</sub>alkyl-;

Het<sup>1</sup> represents a heterocycle selected from piperidinyl, morpholinyl, piperazinyl, furanyl, pyrazolyl, dioxolanyl, thiazolyl, oxazolyl, imidazolyl, isoxazolyl, oxadiazolyl, pyridinyl or pyrrolidinyl wherein said Het<sup>1</sup> is optionally substituted with one or where possible two or more substituents selected from amino, C<sub>1-4</sub>alkyl, hydroxy-C<sub>1-4</sub>alkyl-, phenyl, phenyl-C<sub>1-4</sub>alkyl-, C<sub>1-4</sub>alkyl-oxy-C<sub>1-4</sub>alkyl- mono- or di(C<sub>1-4</sub>alkyl)amino- or amino-carbonyl-;

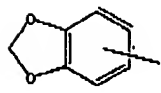
Het<sup>2</sup> represents a heterocycle selected from morpholinyl, piperazinyl, piperidinyl, pyrrolidinyl, thiomorpholinyl or dithianyl wherein said Het<sup>2</sup> is optionally substituted with one or where possible two or more substituents selected from hydroxy, halo, amino, C<sub>1-4</sub>alkyl-, hydroxy-C<sub>1-4</sub>alkyl-, C<sub>1-4</sub>alkyl-oxy-C<sub>1-4</sub>alkyl-, hydroxy-C<sub>1-4</sub>alkyl-oxy-C<sub>1-4</sub>alkyl-, mono- or di(C<sub>1-4</sub>alkyl)amino-, mono- or di(C<sub>1-4</sub>alkyl)amino-C<sub>1-4</sub>alkyl-, aminoC<sub>1-4</sub>alkyl-, mono- or di(C<sub>1-4</sub>alkyl)amino-sulfonyl-, aminosulfonyl-;

Het<sup>3</sup>, Het<sup>4</sup> and Het<sup>8</sup> each independently represent a heterocycle selected from morpholinyl, piperazinyl, piperidinyl, furanyl, pyrazolyl, dioxolanyl, thiazolyl, oxazolyl, imidazolyl, isoxazolyl, oxadiazolyl, pyridinyl or pyrrolidinyl wherein said Het<sup>3</sup>, Het<sup>4</sup> or Het<sup>8</sup> is optionally substituted with one or where possible two or more substituents selected from hydroxy-, amino-, C<sub>1-4</sub>alkyl-, C<sub>3-6</sub>cycloalkyl-C<sub>1-4</sub>alkyl-, aminosulfonyl-, mono- or di(C<sub>1-4</sub>alkyl)aminosulfonyl or amino-C<sub>1-4</sub>alkyl-;

Het<sup>5</sup> represent a heterocycle selected from pyrrolidinyl or piperidinyl wherein said heterocycle is optionally substituted with one or where possible two or more substituents selected from C<sub>1-4</sub>alkyl, C<sub>3-6</sub>cycloalkyl, hydroxy-C<sub>1-4</sub>alkyl-, C<sub>1-4</sub>alkyloxyC<sub>1-4</sub>alkyl or polyhydroxy-C<sub>1-4</sub>alkyl-;

Het<sup>6</sup> and Het<sup>7</sup> each independently represent a heterocycle selected from morpholinyl, pyrrolidinyl, piperazinyl or piperidinyl wherein said Het<sup>6</sup> and Het<sup>7</sup> are optionally substituted with one or where possible two or more substituents selected from C<sub>1-4</sub>alkyl, C<sub>3-6</sub>cycloalkyl, hydroxy-C<sub>1-4</sub>alkyl-, C<sub>1-4</sub>alkyloxyC<sub>1-4</sub>alkyl or polyhydroxy-C<sub>1-4</sub>alkyl-;

Het<sup>9</sup> and Het<sup>10</sup> each independently represent a heterocycle selected from furanyl, piperidinyl, morpholinyl, piperazinyl, pyrazolyl, dioxolanyl, thiazolyl, oxazolyl, imidazolyl, isoxazolyl, oxadiazolyl, pyridinyl or pyrrolidinyl wherein said Het<sup>9</sup> or Het<sup>10</sup> is optionally substituted C<sub>1-4</sub>alkyl, C<sub>3-6</sub>cycloalkyl-C<sub>1-4</sub>alkyl- or amino-C<sub>1-4</sub>alkyl-;

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Het<sup>11</sup> represents a heterocycle selected from indolyl or

Het<sup>12</sup> represents a heterocycle selected from morpholinyl, piperazinyl, piperidinyl, pyrrolidinyl, thiomorpholinyl or dithianyl wherein said Het<sup>12</sup> is optionally substituted with one or where possible two or more substituents selected from hydroxy, halo, amino, C<sub>1-4</sub>alkyl-, hydroxy-C<sub>1-4</sub>alkyl-, C<sub>1-4</sub>alkyl-oxy-C<sub>1-4</sub>alkyl-, hydroxy-C<sub>1-4</sub>alkyl-oxy-C<sub>1-4</sub>alkyl-, mono- or di(C<sub>1-4</sub>alkyl)amino- or mono- or di(C<sub>1-4</sub>alkyl)amino-C<sub>1-4</sub>alkyl-;

Het<sup>13</sup> represent a heterocycle selected from pyrrolidinyl or piperidinyl wherein said heterocycle is optionally substituted with one or where possible two or more substituents selected from C<sub>1-4</sub>alkyl, C<sub>3-6</sub>cycloalkyl, hydroxy-C<sub>1-4</sub>alkyl-, C<sub>1-4</sub>alkyloxyC<sub>1-4</sub>alkyl or polyhydroxy-C<sub>1-4</sub>alkyl-;

Het<sup>14</sup> represent a heterocycle selected from morpholinyl, pyrrolidinyl, piperazinyl or piperidinyl wherein said heterocycle is optionally substituted with one or where possible two or more substituents selected from C<sub>1-4</sub>alkyl, C<sub>3-6</sub>cycloalkyl, hydroxy-C<sub>1-4</sub>alkyl-, C<sub>1-4</sub>alkyloxyC<sub>1-4</sub>alkyl or polyhydroxy-C<sub>1-4</sub>alkyl-;

Het<sup>15</sup> and Het<sup>21</sup> each independently represent a heterocycle selected from morpholinyl, pyrrolidinyl, piperazinyl or piperidinyl wherein said Het<sup>15</sup> or Het<sup>21</sup> are optionally substituted with one or where possible two or more substituents selected from C<sub>1-4</sub>alkyl, C<sub>3-6</sub>cycloalkyl, hydroxy-C<sub>1-4</sub>alkyl-, C<sub>1-4</sub>alkyloxyC<sub>1-4</sub>alkyl or polyhydroxy-C<sub>1-4</sub>alkyl-;

Het<sup>16</sup> represent a heterocycle selected from morpholinyl, pyrrolidinyl, piperazinyl, 1,3,2-dioxaborolane or piperidinyl wherein said heterocycle is optionally substituted with one or more substituents selected from C<sub>1-4</sub>alkyl;

Het<sup>17</sup> represent a heterocycle selected from pyrrolidinyl or piperidinyl wherein said heterocycle is optionally substituted with one or where possible two or more substituents selected from C<sub>1-4</sub>alkyl, C<sub>3-6</sub>cycloalkyl, hydroxy-C<sub>1-4</sub>alkyl-, C<sub>1-4</sub>alkyloxyC<sub>1-4</sub>alkyl or polyhydroxy-C<sub>1-4</sub>alkyl-;

Het<sup>18</sup> and Het<sup>19</sup> each independently represent a heterocycle selected from morpholinyl, pyrrolidinyl, piperazinyl or piperidinyl wherein said Het<sup>18</sup> and Het<sup>19</sup> are optionally substituted with one or where possible two or more substituents selected from C<sub>1-4</sub>alkyl, C<sub>3-6</sub>cycloalkyl, hydroxy-C<sub>1-4</sub>alkyl-, C<sub>1-4</sub>alkyloxyC<sub>1-4</sub>alkyl or polyhydroxy-C<sub>1-4</sub>alkyl-;

Het<sup>20</sup> represents a heterocycle selected from pyrrolidinyl, 2-pyrrolidinyl, piperidinyl, piperazinyl or pyrazolidinyl wherein said heterocycle is optionally substituted with one or where possible two or more substituents selected from C<sub>1-4</sub>alkyl,

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C<sub>3-6</sub>cycloalkyl, hydroxy-C<sub>1-4</sub>alkyl-, C<sub>1-4</sub>alkyloxyC<sub>1-4</sub>alkyl or polyhydroxy-C<sub>1-4</sub>alkyl-; and

Ar<sup>1</sup>, Ar<sup>2</sup>, Ar<sup>3</sup>, Ar<sup>4</sup> and Ar<sup>5</sup> each independently represent phenyl optionally substituted with cyano, C<sub>1-4</sub>alkylsulfonyl-, C<sub>1-4</sub>alkylsulfonylamino-, aminosulfonylamino-, hydroxy-C<sub>1-4</sub>alkyl, aminosulfonyl-, hydroxy-, C<sub>1-4</sub>alkyloxy- or C<sub>1-4</sub>alkyl.

2. (Original) A compound according to claim 1 wherein;

Z represents NH;

Y represents -C<sub>3-9</sub>alkyl-, -C<sub>2-9</sub>alkenyl-, -C<sub>1-5</sub>alkyl-oxy-C<sub>1-5</sub>alkyl-, -C<sub>1-5</sub>alkyl-NR<sup>13</sup>-C<sub>1-5</sub>alkyl-, -C<sub>1-5</sub>alkyl-NR<sup>14</sup>-CO-C<sub>1-5</sub>alkyl-, -C<sub>1-6</sub>alkyl-NH-CO-, -CO-C<sub>1-7</sub>alkyl-, -C<sub>1-7</sub>alkyl-CO- or C<sub>1-6</sub>alkyl-CO-C<sub>1-6</sub>alkyl;

X<sup>1</sup> represents O, -O-C<sub>1-2</sub>alkyl-, -O-N=CH-, NR<sup>11</sup> or -NR<sup>11</sup>-C<sub>1-2</sub>alkyl-; in a particular embodiment X<sup>1</sup> represents a direct bond, C<sub>1-2</sub>alkyl-, -O-C<sub>1-2</sub>alkyl-, -NR<sup>11</sup>-, -O- or -O-CH<sub>2</sub>-;

X<sup>2</sup> represents a direct bond, O, -O-C<sub>1-2</sub>alkyl-, -O-N=CH-, NR<sup>17</sup>-CO-, NR<sup>17</sup>-CO-C<sub>1-2</sub>alkyl-, C<sub>1-2</sub>alkyl, Het<sup>20</sup>-C<sub>1-2</sub>alkyl-, NR<sup>12</sup> or NR<sup>12</sup>-C<sub>1-2</sub>alkyl-; in a particular embodiment X<sup>2</sup> represents a direct bond, C<sub>1-2</sub>alkyl-, -O-C<sub>1-2</sub>alkyl, NR<sup>17</sup>-CO-, NR<sup>17</sup>-CO-C<sub>1-2</sub>alkyl-, Het<sup>20</sup>-C<sub>1-2</sub>alkyl-, -O- or -O-CH<sub>2</sub>-;

R<sup>1</sup> represents hydrogen, cyano, halo or hydroxy, preferably halo;

R<sup>2</sup> represents hydrogen, cyano, halo, hydroxy, hydroxycarbonyl-, C<sub>1-4</sub>alkyloxycarbonyl-, Het<sup>16</sup>-carbonyl-, C<sub>1-4</sub>alkyl-, C<sub>2-6</sub>alkynyl-, Ar<sup>5</sup> or Het<sup>1</sup>; in a further embodiment R<sup>2</sup> represents hydrogen, cyano, halo, hydroxy, or Ar<sup>5</sup>; in a more particular embodiment R<sup>2</sup> represents hydrogen or halo;

R<sup>3</sup> represents hydrogen;

R<sup>4</sup> represents hydrogen, hydroxy, C<sub>1-4</sub>alkyloxy-, Ar<sup>4</sup>-C<sub>1-4</sub>alkyloxy or R<sup>4</sup> represents C<sub>1-4</sub>alkyloxy substituted with one or where possible two or more substituents selected from C<sub>1-4</sub>alkyloxy- or Het<sup>2</sup>-;

R<sup>11</sup> represents hydrogen, C<sub>1-4</sub>alkyl- or C<sub>1-4</sub>alkyl-oxy-carbonyl-;

R<sup>12</sup> represents hydrogen, C<sub>1-4</sub>alkyl- or C<sub>1-4</sub>alkyl-oxy-carbonyl-;

R<sup>13</sup> represents hydrogen or Het<sup>14</sup>-C<sub>1-4</sub>alkyl, in particular morpholinyl-C<sub>1-4</sub>alkyl;

R<sup>14</sup> represents hydrogen or C<sub>1-4</sub>alkyl;

R<sup>17</sup> represents hydrogen, C<sub>1-4</sub>alkyl-, Het<sup>21</sup>-C<sub>1-4</sub>alkyl or C<sub>1-4</sub>alkyl-oxy-C<sub>1-4</sub>alkyl; in particular R<sup>17</sup> represents hydrogen or C<sub>1-4</sub>alkyl;

Het<sup>1</sup> represents thiazolyl optionally substituted with amino, C<sub>1-4</sub>alkyl, hydroxy-C<sub>1-4</sub>alkyl-, phenyl, phenyl-C<sub>1-4</sub>alkyl-, C<sub>1-4</sub>alkyl-oxy-C<sub>1-4</sub>alkyl-, mono- or di(C<sub>1-4</sub>alkyl)amino- or amino-carbonyl-;

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Het<sup>2</sup> represents a heterocycle selected from morpholinyl, piperazinyl, piperidinyl or pyrrolidinyl wherein said Het<sup>2</sup> is optionally substituted with one or where possible two or more substituents selected from hydroxy, amino or C<sub>1-4</sub>alkyl-;

In a further embodiment Het<sup>2</sup> represents a heterocycle selected from morpholinyl or piperidinyl optionally substituted with C<sub>1-4</sub>alkyl-, preferably methyl;

Het<sup>14</sup> represents a heterocycle selected from morpholinyl, piperazinyl, piperidinyl or pyrrolidinyl wherein said Het<sup>14</sup> is optionally substituted with one or where possible two or more substituents selected from hydroxy, amino or C<sub>1-4</sub>alkyl-;

Het<sup>16</sup> represents a heterocycle selected from piperidinyl, morpholinyl or pyrrolidinyl;

Het<sup>20</sup> represents a heterocycle selected from pyrrolidinyl, 2-pyrrolidinyl or piperidinyl;

Het<sup>21</sup> represents a heterocycle selected from morpholinyl, piperazinyl, piperidinyl or pyrrolidinyl wherein said Het<sup>21</sup> is optionally substituted with one or where possible two or more substituents selected from hydroxy, amino or C<sub>1-4</sub>alkyl-;

Ar<sup>4</sup> represents phenyl optionally substituted with cyano, hydroxy-, C<sub>1-4</sub>alkyloxy or C<sub>1-4</sub>alkyl-;

Ar<sup>5</sup> represents phenyl optionally substituted with cyano, hydroxy, C<sub>1-4</sub>alkyloxy or C<sub>1-4</sub>alkyl.

3. (Original) A compound according to claim 1 wherein;

Z represents NH;

Y represents -C<sub>3-9</sub>alkyl-, -C<sub>1-5</sub>alkyl-NR<sup>13</sup>-C<sub>1-5</sub>alkyl-, -C<sub>1-5</sub>alkyl-NR<sup>14</sup>-CO-C<sub>1-5</sub>alkyl-, -C<sub>1-6</sub>alkyl-NH-CO- or -CO-NH-C<sub>1-6</sub>alkyl-;

X<sup>1</sup> represents -O-, -NR<sup>11</sup>-, -NR<sup>16</sup>-CO-, or -NR<sup>16</sup>-CO-C<sub>1-2</sub>alkyl-;

X<sup>2</sup> represents a direct bond, -C<sub>1-2</sub>alkyl-, -O-C<sub>1-2</sub>alkyl-, -O-, -O-CH<sub>2</sub>- or Het<sup>20</sup>-C<sub>1-2</sub>alkyl-;

R<sup>1</sup> represents hydrogen or halo;

R<sup>2</sup> represents hydrogen, cyano, halo, hydroxycarbonyl-, C<sub>1-4</sub>alkyloxycarbonyl-, Het<sup>16</sup>-carbonyl- or Ar<sup>5</sup>; in particular R<sup>2</sup> represents hydrogen or halo;

R<sup>3</sup> represents hydrogen;

R<sup>4</sup> represents hydrogen, hydroxy, C<sub>1-4</sub>alkyloxy-, Ar<sup>4</sup>-C<sub>1-4</sub>alkyloxy or R<sup>4</sup> represents C<sub>1-4</sub>alkyloxy substituted with one or where possible two or more substituents selected from C<sub>1-4</sub>alkyloxy- or Het<sup>2</sup>-;

R<sup>11</sup> represents hydrogen;

R<sup>12</sup> represents hydrogen, C<sub>1-4</sub>alkyl- or C<sub>1-4</sub>alkyl-oxy-carbonyl-;

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R<sup>13</sup> represents hydrogen or Het<sup>14</sup>-C<sub>1-4</sub>alkyl, in particular hydrogen or morpholinyl-C<sub>1-4</sub>alkyl;

Het<sup>2</sup> represents a heterocycle selected from morpholinyl, piperazinyl, piperidinyl or pyrrolidinyl wherein said Het<sup>2</sup> is optionally substituted with one or where possible two or more substituents selected from hydroxy, amino or C<sub>1-4</sub>alkyl-;

In a further embodiment Het<sup>2</sup> represents a heterocycle selected from morpholinyl or piperidinyl optionally substituted with C<sub>1-4</sub>alkyl-, preferably methyl;

Het<sup>14</sup> represents morpholinyl;

Het<sup>16</sup> represents a heterocycle selected from morpholinyl or pyrrolidinyl;

Het<sup>20</sup> represents pyrrolidinyl or piperidinyl;

Ar<sup>4</sup> represents phenyl;

Ar<sup>5</sup> represents phenyl optionally substituted with cyano.

4. (Previously presented) A compound according to claim 1 wherein the R<sup>1</sup> substituent is at position 4', the R<sup>2</sup> substituent is at position 5', the R<sup>3</sup> substituent is at position 3 and the R<sup>4</sup> substituent at position 7 of the structure of formula (I).

5. (Previously presented) A compound according to claim 1, wherein a<sup>1</sup>-a<sup>2</sup>=a<sup>3</sup>-a<sup>4</sup> represents N-CH=CH-CH.

6.-11. (Cancelled)

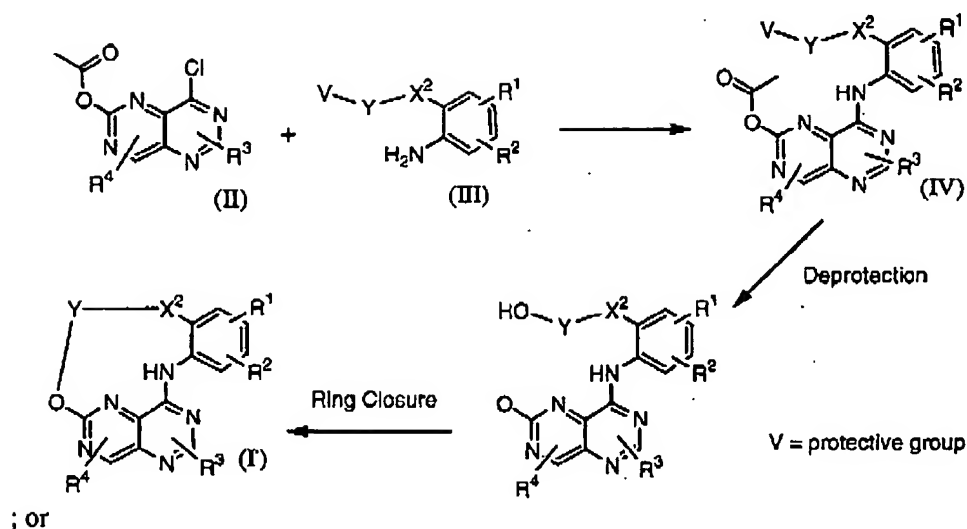
12. (Previously presented) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and, as active ingredient, an effective kinase inhibitory amount of a compound as claimed in claim 1.

13-15. (Cancelled)

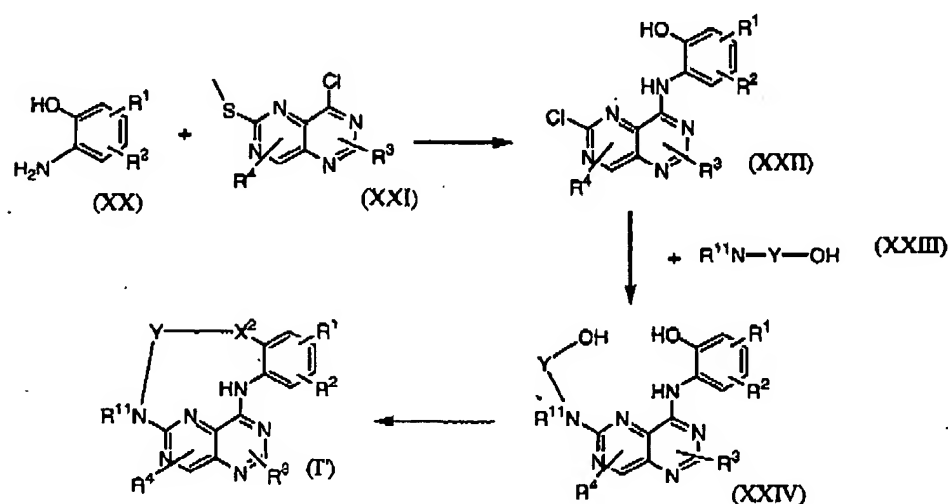
16. (Amended) A process for preparing a compound as claimed in claims 1-to-7, comprising;

a) coupling 2-acetoxy-8-chloropyrimido[5,4-d]pyrimidine derivatives (II) with suitable substituted anilines (III), to furnish the intermediates of formula (IV), and deprotecting the intermediates of formula (IV) followed by ring closure under suitable conditions;

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b) coupling the known 8-chloro-2(methylthio)-pyrimido[5,4-d]pyrimidine with 2-aminophenol derivatives of formula (XXI), yielding the intermediate compounds of formula (XXII), followed by activating the pyrido[3,2-d]pyrimidine of formula (XXII) using an aminated alcohol (XXIII) under art known conditions, followed by ring closure under Mitsunobu conditions to give the target compounds of formula (I').



17. (Cancelled)

18. (Cancelled)